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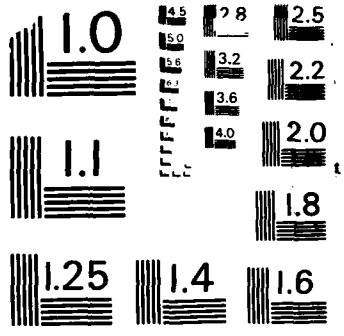

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ATROPINE AND HUMAN CONTRAST SENSITIVITY FUNCTION

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Letterman Army Institute of Research

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Atropine and human contrast sensitivity function--Penetar and Kearney

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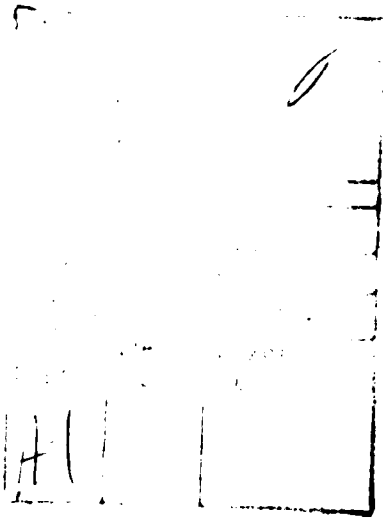
PREFACE

We express appreciation to physicians CPT Peter Maningas, MAJ Donald Marks, and MAJ William Bickell, whose assistance was crucial to the completion of this experiment and to the health and safety of the volunteers. We thank SGT Sally Ruiz and SGT Helen Ford for their skillful technical assistance, and Dr. Virginia Gildengorin and Mr. Jerome Volchany for their assistance with the statistical analysis of the data. Most of all, we express appreciation to the volunteers who willingly bore the atropine effects.

ABSTRACT

The effects of one and two autoinjector equivalents of atropine sulfate (2 and 4 mg/70 kg im) on contrast sensitivity were measured in eight male volunteers, ages 22 to 39 yr. Using an automated contrast sensitivity machine, volunteers were required to detect sinusoidal gratings of 0.5, 1.0, 3.0, 6.0, 11.4, and 22.8 cycles per degree. At two hr after injection, no atropine effect was observed for any frequency.



INTRODUCTION

Atropine is a potent and long-lasting anticholinergic agent. Its mydriatic and cycloplegic effects on visual acuity and accommodation have been studied. Recently Baker (1) and Jampolsky (2) and colleagues reported that following injections of 2 and 4 mg of atropine per 70 kg of body weight there was no effect on either high or low contrast visual acuity at a distance of 20 feet. On the other hand, low-contrast visual acuity at 40 cm is affected by 4 mg atropine per 70 kg. These visual effects had a relatively slow onset and were long-lasting, beginning about 4 hours after injection and persisting for at least 7 hours after injection. Recovery was observed the following day.

Visual acuity may be closely correlated with the ability to resolve targets of high spatial frequency. Measurements of visual acuity do not provide information on the ability to resolve low and mid-range spatial frequency details. Many military tasks, such as detection and tracking of vehicles, require resolution in these spatial frequency ranges.

The contrast sensitivity function measures at a fixed luminance the minimum amount of contrast between target and background required for discrimination of targets across the spatial frequency spectrum. It is the reciprocal of the threshold contrast. Measurement of the contrast sensitivity function makes it possible to characterize a broad range of visual functions rather than define only the upper boundary of spatial resolution.

Measurement of the contrast sensitivity function has been employed in studies on the effects of 2 and 4 mg/70 kg doses of atropine in humans. Four hours after a 2 mg/70 kg dose of atropine, a small but consistent loss in sensitivity was found at all spatial frequencies, when tested at a distance of 40 cm. Significant decrements were found only for spatial frequencies of 5 and 20 cycles per degree (1). In another study frequencies between 3 and 7 cycles per degree were not affected by a dose of 4 mg/70 kg (3).

Although these studies show that atropine affects contrast sensitivity when tested at reading distances (40 cm), they do not address the question of atropine effects on distance (ie 20 ft and beyond) contrast sensitivity. The nature of the contrast sensitivity function after atropine for distances beyond 40 cm has important military consequences as soldiers are required to resolve targets at distances well beyond this distance.

It has been observed that atropine's maximum effect on pursuit tracking performance occurs in parallel to its maximum effect on pupil size and accommodation and does not correspond to this drug's maximum cardiovascular effects (3). The tracking task is done at optical infinity and the reasons for the observed tracking decrements are unlikely to be due to pupil and accommodative changes alone. Changes in distance contrast sensitivity may be a factor. Therefore, during a recent field evaluation of atropine's effects on tracking (4), we also measured distance contrast sensitivity on a broader range of spatial frequencies than previously reported.

METHODS

Participants: Eight male volunteers between the ages of 22 and 39 were selected for this study. All were in excellent health. They all had either uncorrected visual acuity of 20/20, or were correctable to 20/20 with spectacle lenses. Most were emmetropic or had an error of refraction within 1 diopter of emmetropia. One volunteer had a refractive error of 3 diopters myopia. Ophthalmoscopy, tonometry and slit lamp examination were normal. Corrective spectacles were worn by those volunteers whose distance visual acuity was less than 20/20.

Procedures: The contrast sensitivity function was measured using a Nicolet CS-2000 test system. Threshold determinations were made for six frequencies: 0.5, 1.0, 3.0, 6.0, 11.4, and 22.8 cycles per degree. The test was conducted in a bright interior environment, with no direct sunlight. Volunteers viewed a 13 inch black and white TV monitor from a distance of 10 feet. The display contrast began at 0 and increased under computer control. Volunteers were required to press a button when they detected the appearance of a sinusoidal grating. Each frequency was presented five times and the mean log threshold contrast was recorded. This method is similar to an ascending method of limits psychophysical procedure.

Contrast sensitivity functions were generated for each individual for four drug conditions: 1) baseline (no drug), 2) saline placebo, 3) 2 mg/70 kg, and 4) 4 mg/70 kg atropine sulfate. Injections were given intramuscularly 2 hours before testing in a double masked fashion. Order was counterbalanced across volunteers. Data were analyzed by means of a 2-way repeated measures analysis of variance (BMDP-2V) (5). Separate ANOVAs were performed on the data for each spatial frequency.

RESULTS

Contrast sensitivity function for each injection condition across the frequencies tested is shown (Figure). The shape of the function observed under baseline condition is typical of normal human functioning. Differences across frequencies are highly significant ($F=10.27$, $df=5,35$, $p<0.0000$), confirming the fact that humans are differentially sensitive to frequencies within the range tested. Peak sensitivity occurs within the 5 to 8 cycles/degree range with considerable less sensitivity at frequencies higher or lower.

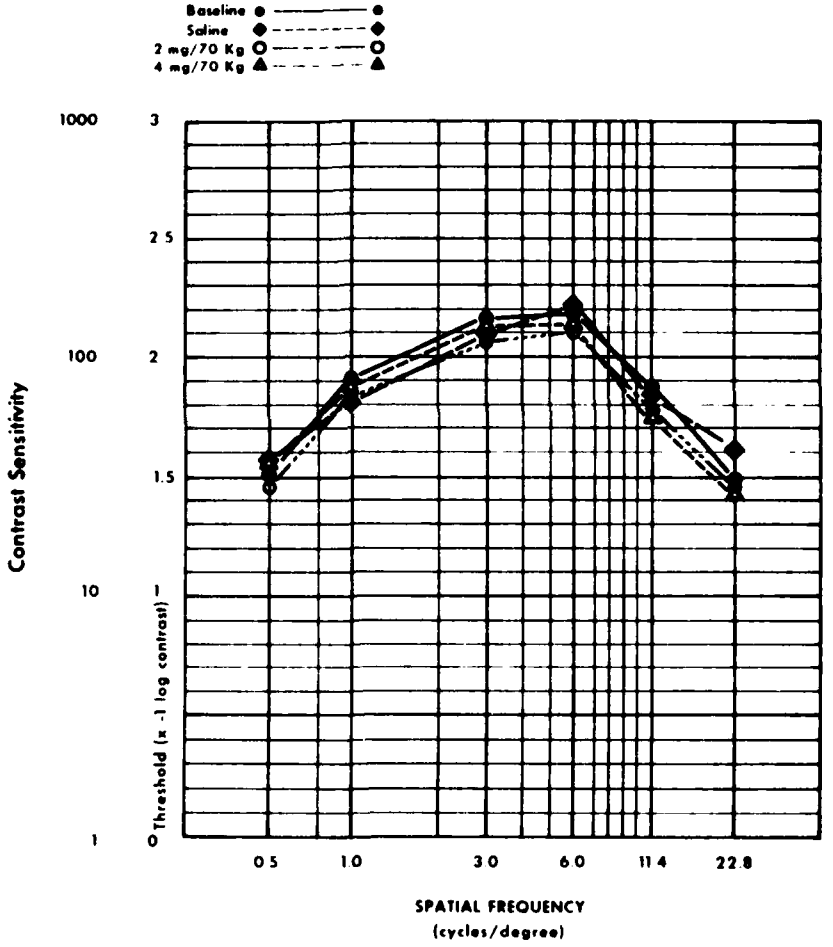


Figure. Contrast sensitivity functions for four drug conditions 2 hr after injection.

Inspection of the figure suggests differences among the injection conditions, especially at frequencies 3 cycles per degree and above. The largest differences were observed at 22 cycles per degree. All observed differences were small and nonsignificant, however ($F=0.77$, $df=3,21$, $p<0.5258$).

DISCUSSION

Previous reports have shown anticholinergic effects on contrast sensitivity using other tests (1,3,6). Other researchers using the same apparatus found a significant effect with 4 mg/70 kg atropine. Behar reported a reduction of up to 50% in sensitivity at frequencies of 3, 9, and 16 cycles/degree (7). These findings are not in conformity with our results, and additional research is indicated to explain this discrepancy.

The effects of atropine on vision may be due to a decrease in the amplitude of accommodation or to the reduced optical quality of the image seen through an enlarged pupil. The loss in visual function due to reduced accommodation is most apparent for near vision and in the case of uncorrected hyperopia. Three hours after a dose of 4 mg/70 kg of atropine, one would expect an accommodative loss of almost 3.5 diopters (2). Recovery of accommodation is incomplete at 24 hours. Full recovery is not seen until 48 hours following injection.

One should not expect a reduction in distance visual function in subjects who either are emmetropic or are rendered emmetropic by the use of spectacles, or who are uncorrected myopes. The amount of accommodation required at our test distance is approximately 0.33 diopters, a very small amount, and one not expected to produce a significant visual loss.

Atropine-induced visual loss at our experimental distances is secondary to optical aberrations accompanying mydriasis. These include the veiling glare effect of the increased light transmitted to the retina, increased scatter as more light passes through the crystalline lens, and decrease in the point spread function. These aberrations are secondary to the imperfections of the crystalline lens as an optical medium. Other mechanisms include effects on the neural pathways of vision and the overall malaise experienced by persons who receive moderate to high dosages of anticholinergic drugs.

Our results indicate that under these conditions the visual system remains essentially intact. Perhaps a significant loss would be encountered under different conditions, such as performance of the test outdoors in bright sunlight or in an environment where glare from additional sources is present.

The contrast sensitivity function measures overall visual function. It is useful in assessing drug and other physiological and environmental effects. Altered thresholds may affect a soldier's ability to perform adequately in the field when required to detect and identify landmarks or camouflaged targets. If the growing threat of chemical weapons is to be countered with drugs such as atropine, an in-depth analysis of this and other anticholinergic drugs' effects on vision must proceed in both the laboratory and the field.

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